

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A haemostatic composition ~~sponge, powder or flakes~~ comprising gelatin[[e]] ~~or collagen~~[[,]] and hyaluronic acid (HA)₂ or a derivative thereof, wherein said hyaluronic acid (HA)₂ or a derivative thereof₂ is incorporated into said composition ~~sponge, powder or flakes~~ to a final content of at least 10% (w/w).
2. (Canceled)
3. (Currently amended) The haemostatic composition ~~sponge, powder or flakes~~ according to claim 1[[2]], wherein said hyaluronic acid (HA)₂ derivative is a salt or an ester of hyaluronic acid (HA)₂.
4. (Canceled)
5. (Currently amended) The haemostatic composition ~~sponge, powder or flakes~~ according to claim 1, wherein said composition comprises ~~at the most 99% (w/w) of said gelatin or collagen, at the most 95% (w/w) of said gelatin or collagen, at the most 90% (w/w) of said gelatin or collagen, at the most 85% (w/w) of said gelatin or collagen, at the most 80% (w/w) of said gelatin or collagen, at the most 75% (w/w) of said gelatin or collagen, at the most 70% (w/w) of said gelatin or collagen, at the most 65% (w/w) of said gelatin or collagen, or at the most 60% (w/w) of said gelatin or collagen.~~
6. (Currently amended) The haemostatic composition ~~sponge, powder or flakes~~ according to claim 1, further comprising at least one blood coagulation factor, wherein said blood coagulation factor is selected from the group consisting of thrombin or a precursor thereof, factor Va, factor VIIa, factor VIIIa, factor IXa, factor Xa, factor XIa, factor XIIa, factor XIIIa and calcium ions.

7. (Currently amended) The haemostatic composition ~~sponge, powder or flakes~~ according to claim 6, further comprising a thrombin-stabilising agent selected from the group consisting of naturally occurring amino acids, mono-, di- or polysaccharides, polyglycols, proteins and mixtures thereof.
8. (Currently amended) The haemostatic composition ~~sponge, powder or flakes~~ according to claim 1, further comprising at least one anti-fibrinolytic agent, wherein said anti-fibrinolytic agent is selected from the group consisting of aprotinin, pepstatin, leupeptin, antipain, chymostatin, gabexate mesilate, fibronectin, ϵ -amino caproic acid and tranexamic acid.
9. (Canceled)
10. (Currently amended) The haemostatic composition ~~sponge, powder or flakes~~ according to claim 1, wherein said composition is in the form of a haemostatic sponge, wherein said sponge absorbs less water than an absorbable gelatin sponge.
11. (Currently amended) The haemostatic composition ~~sponge~~ according to claim 10, wherein the ratio between the water absorbed by ~~a~~ the haemostatic sponge ~~according to claim 1~~ and the water absorbed by an absorbable gelatin sponge is at the most 0.95 when determined in accordance with USP 24.
12. (Canceled)
13. (Canceled)
14. (Currently amended) The haemostatic composition ~~sponge~~ according to claim 1, wherein said composition is in the form of a haemostatic sponge, wherein at least one of the surfaces of the haemostatic sponge is covered by a top sheet.
15. (Currently amended) The haemostatic composition ~~sponge~~ according to claim 14, wherein the top sheet is removable.

16. (Canceled)

17. (Currently amended) The haemostatic composition ~~sponge, powder or flakes~~ according to claim 1, wherein said composition is dry.

18. (Currently amended) A haemostatic paste prepared by pre-wetting the haemostatic composition ~~powder or flakes~~ according to claim 1 with a liquid to create said a paste.

19. (Currently amended) A method ~~for~~ of promoting haemostasis in an individual in need thereof, said method comprising the step of applying the haemostatic composition ~~sponge, powder or flakes of~~ according to claim 1, or the paste according to claim 18, onto at least a portion of an area where bleeding is present.

20. (Canceled)

21. (Currently amended) A method of delivering an agent to an intended local site of a patient, said method comprising the step of including the agent in the composition ~~sponge, powder or flakes~~ of claim 1, or in the paste of claim 18, and delivering the agent to the local site of the patient.

22. (Currently amended) A method for arresting bleeding in an individual in need thereof, said method comprising the step of applying to the site of bleeding the haemostatic composition ~~sponge, powder or flakes~~ according to claim 1 or the paste according to claim 18.

23. (Currently amended) A method ~~for~~ producing a haemostatic composition comprising the steps of:

i) mixing a biologically absorbable material and hyaluronic acid or a derivative thereof, and a solvent, and

ii) treating the mixture obtained in step i) with dry heat at a temperature between 110-200°C.

24. (Currently amended) TheA method according to claim 23, wherein said method comprises a further step of drying the mixture obtained in step i) before treating the mixture with dry heat at a temperature between 110-200°C according to step ii).

25. (Canceled)

26. (Canceled)

27. (Currently amended) A method for preparing the haemostatic composition ~~sponge~~ according to claim 17, said method comprising the steps of:

- i) mixing gelatin ~~a biologically absorbable material~~, hyaluronic acid (HA), or a derivative thereof, and a solvent; and
- ii) drying said mixture.

28. (Currently amended) TheA method according to claim 27, wherein said method further comprises a step of stabilising the mixture obtained in said step ii) ~~or the sponge~~.

29. (Currently amended) A method according to ~~any of~~ claims 23 ~~or 27~~, wherein the mixing of the biologically absorbable material, hyaluronic acid (HA), or a derivative thereof, and a solvent ~~is may be~~ performed by any of the following alternatives:

- a) mixing a biologically absorbable material with hyaluronic acid (HA) or a derivative thereof and subsequently adding a solvent;
- b) mixing a solution of a biologically absorbable material with a solution of hyaluronic acid (HA) or a derivative thereof;
- c) mixing a biologically absorbable material with a solution of hyaluronic acid (HA) or a derivative thereof;
- d) mixing a solution of a biologically absorbable material with hyaluronic acid (HA) or a derivative thereof.

30. (Previously presented) The method according to any of claims 23 or 27, wherein said mixing is performed under mechanical influence.
31. (Canceled)
32. (Canceled)
33. (Currently amended) ~~The~~A method according to claim 28, wherein said step of stabilising the mixture obtained in said step ii) comprises treating the mixture ~~or sponge~~ with dry heat at a temperature between 110-200°C or treating ~~it~~the mixture with a compound capable of chemically cross-linking the mixture ~~or sponge~~.
34. (Currently amended) ~~The~~A method according to any of claims 23 or 27, wherein said method further comprises a step of sterilization of the mixture ~~or sponge~~.
35. (Currently amended) ~~The~~A method according to ~~any of~~ claims 23 ~~or 27~~, wherein the biologically absorbable material is selected from the group consisting of gelatin ~~gelatine~~, collagen, chitin, chitosan, alginate, cellulose, oxidised cellulose, oxidised regenerated cellulose, carboxymethylcellulose (CMC), hydroxyethylcellulose (HEC), polyglycolic acid, polyacetic acid, derivatives thereof and mixtures thereof.
36. (Currently amended) The method according to any of claims 23 or 27, wherein said ~~solution of~~ hyaluronic acid (HA), or a derivative thereof, is provided in the form of a gel.
37. (Previously presented) The method according to any of claims 24 or 27, wherein said drying is performed at a temperature from about 20°C to about 40°C, or at about 30°C.
38. (Currently amended) The method according to any of claims 24 or 27, wherein said drying is conducted for about 6 to about 24 hours, or ~~at~~ for about 16 hours.

39. (Previously presented) The method according to any of claims 24 or 27, wherein said drying is performed by freeze-drying.
40. (Currently amended) A haemostatic composition ~~obtainable by a method according to claim 23~~ obtained by a method comprising the steps of:
- i) mixing a biologically absorbable material and hyaluronic acid (HA), or a derivative thereof, and a solvent, and
 - ii) treating the mixture obtained in step i) with dry heat at a temperature between 110-200°C.
41. (Previously presented) The method according to any of claims 23 or 27 wherein said mixing is performed by whipping, stirring, spinning, static mixing, motionless mixing or centrifugation.
42. (New) A haemostatic composition comprising gelatin and hyaluronic acid (HA), or a derivative thereof, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition by cross-linking by using dry heat at 110-200°C.
43. (New) The haemostatic composition according to claim 42, wherein said gelatin and hyaluronic acid (HA) are cross-linked by using dry heat at 110-200°C.
44. (New) A haemostatic composition comprising gelatin and hyaluronic acid (HA), or a derivative thereof, wherein said composition does not comprise collagen.
45. (New) A haemostatic composition comprising gelatin and hyaluronic acid (HA), or a derivative thereof, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition and wherein the hyaluronic acid (HA), or derivative thereof, has a molecular weight of from 1,500 to 5,000 kDa.
46. (New) The haemostatic composition according to any of claims 1, 42 or 45 further comprising an additional component selected from the group consisting of collagen, chitin,

chitosan, alginate, cellulose, oxidised cellulose, oxidised regenerated cellulose, carboxymethylcellulose (CMC), hydroxyethylcellulose (HEC), polyglycolic acid or polyacetic acid, derivatives thereof and mixtures thereof.

47. (New) The haemostatic composition according to any of claims 1, 42 or 45, wherein said composition does not comprise collagen.

48. (New) The haemostatic composition according to claim 5, wherein said amount of gelatin is at the most 85% (w/w).

49. (New) The haemostatic composition according to claim 5, wherein said amount of gelatin is at the most 80% (w/w).

50. (New) The haemostatic composition according to claim 5, wherein said amount of gelatin is at the most 75% (w/w).

51. (New) The haemostatic composition according to claim 5, wherein said amount of gelatin is at the most 70% (w/w).

52. (New) The haemostatic composition according to claim 5, wherein said amount of gelatin is at the most 65% (w/w).

53. (New) The haemostatic composition according to claim 5, wherein said amount of gelatin is at the most 60% (w/w).

54. (New) The haemostatic composition according to claim 1, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition to a final content of at least 15% (w/w).

55. (New) The haemostatic composition according to claim 1, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition to a final content of at least 20% (w/w).

56. (New) The haemostatic composition according to claim 1, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition to a final content of at least 25% (w/w).

57. (New) The haemostatic composition according to claim 1, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition to a final content of at least 30% (w/w).

58. (New) The haemostatic composition according to claim 1, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition to a final content of at least 35% (w/w).

59. (New) The haemostatic composition according to claim 1, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition to a final content of at least 40% (w/w).

60. (New) The haemostatic composition according to claim 1, wherein the hyaluronic acid (HA) is chemically cross-linked.

61. (New) The haemostatic composition according to claim 1, wherein the hyaluronic acid (HA) is physically cross-linked.

62. (New) The haemostatic composition according to claim 1, wherein the hyaluronic acid (HA) has a pH value in the range of from 5 to 9.

63. (New) The haemostatic composition according to claim 1, wherein the hyaluronic acid (HA) derivative can be selected from the group consisting of esters of hyaluronic acid,

hyaluronate salts of hyaluronic acid, hyaluronic acid salified with organic bases, hyaluronic acid salified with inorganic bases, hyaluronic acid salified with organic and/or inorganic bases, Hyaff®, hyaluronic acid esters with alcohols of the aliphatic, araliphatic, cycloaliphatic, aromatic, cyclic and heterocyclic series, with an esterification degree that may vary depending on the type and length of the alcohol used, Hyadd®, amides of hyaluronic acid with amines of the aliphatic, araliphatic, cycloaliphatic, aromatic, cyclic and heterocyclic series, with an amidation degree that may vary depending on the type and length of the amine used, Hyox®[®], percarboxylated hyaluronic acid derivatives obtained by oxidation of the primary hydroxyl group of the N-acetyl-D-glucosamine unit, deacetylates of hyaluronic acid, and O-sulphated hyaluronic acid derivatives.

64. (New) The haemostatic composition according to claim 1, which further comprises a buffering agent, wherein said buffering agent is selected from the group consisting of alkaline metal salts, acetates, citrates, phosphates, hydrogen phosphates, carbonates, hydrogen carbonates, succinates, imidazole, TRIS, and zwitteranionic buffering systems.

65. (New) The haemostatic composition according to claim 1, which further comprises one or more antimicrobial agent(s).

66. (New) The haemostatic composition according to claim 65, wherein the one or more antimicrobial agent(s) comprises one or more antibacterial agent(s).

67. (New) The haemostatic composition according to claim 66, wherein the one or more antibacterial agent(s) comprises one or more antibiotic(s).

68. (New) The haemostatic composition according to claim 67, wherein the one or more antibiotic(s) is selected from the group consisting of β -lactams, penicillins, cephalosporins, monobactams, macrolides, polymyxins, tetracyclines, chloramphenicol, thrimethoprim, aminoglycosides, clindamycin, and metronidazole.

69. (New) The haemostatic composition according to claim 65, wherein the one or more antimicrobial agent(s) comprises one or more sulphonamide(s).
70. (New) The haemostatic composition according to claim 69, wherein the one or more sulphonamide(s) is selected from the group consisting of sulphadimidine and sulphadimethoxin.
71. (New) The haemostatic composition according to claim 65, wherein the one or more antimicrobial agent(s) comprises one or more antimycotic agent(s).
72. (New) The haemostatic composition according to claim 71, wherein the one or more antimycotic agent(s) is selected from the group consisting of amphotericin B, ketoconazol and miconazol.
73. (New) The haemostatic composition according to claim 65, wherein the one or more antimicrobial agent(s) comprises one or more antiviral agent (s).
74. (New) The haemostatic composition according to claim 73, wherein the one or more antiviral agent (s) is idoxuridine and azidothymidin.
75. (New) The haemostatic composition according to claim 65, wherein the one or more antimicrobial agent(s) comprises silver ions or silver ion complexes.
76. (New) The haemostatic composition according to claim 65, wherein the one or more antimicrobial agent(s) comprises tobramycin or a salt thereof.
77. (New) The haemostatic composition according to claim 1, which further comprises one or more anti-infectives.
78. (New) The haemostatic composition according to claim 77, wherein the one or more anti-infectives is selected from the group consisting of halogens, chlorohexidine, quaternary ammonium compounds and triclosan.

79. (New) The haemostatic composition according to claim 1, which further comprises one or more agent(s) selected from the group consisting of surfactants, antiseptics, pain relieving agents, chemotherapeutics, anaesthetics, healing-promoting agents, vitamins, minerals, amino acids, proteins, growth factors, cells, enzymes, contrast agents, preservatives, emulsifiers, cross-linking agents to promote healing and chemotherapeutic agents.

80. (New) The haemostatic composition according to claim 1, which further comprises one or more surfactant(s).

81. (New) The haemostatic composition according to claim 80, wherein the one or more surfactant(s) is selected from the group consisting of anionic surfactants, cationic surfactants, non-ionic surfactants and surface active biological modifiers.

82. (New) The haemostatic composition according to claim 81, wherein the one or more anionic surfactants is selected from the group consisting of potassium laurate, triethanolamine stearate, sodium lauryl sulfate, sodium dodecylsulfate, alkyl polyoxyethylene sulfates, sodium alginate, dioctyl sodium sulfosuccinate, phosphatidyl glycerol, phosphatidyl inositol, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, bile acids and their salts, cholic acid, deoxycholic acid, glycocholic acid, taurocholic acid, glycodeoxycholic acid, and calcium carboxymethylcellulose.

83. (New) The haemostatic composition according to claim 81, wherein the one or more cationic surfactants is selected from the group consisting of quaternary ammonium compounds, benzalkonium chloride, cetyltrimethylammonium bromide, chitosans and lauryldimethylbenzylammonium chloride.

84. (New) The haemostatic composition according to claim 81, wherein the one or more non-ionic surfactants is selected from the group consisting of polyoxyethylene fatty alcohol ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, sorbitan esters, glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol,

cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers, polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polysaccharides, starch, starch derivatives, hydroxyethylstarch, polyvinyl alcohol, and polyvinylpyrrolidone.

85. (New) The haemostatic composition according to claim 79, wherein the one or more preservatives is selected from the group consisting of benzoic acid, sorbic acid, parabens, methyl-p- hydroxy benzoic acid, ethyl-p-hydroxy benzoic acid, propyl-p-hydroxy benzoic acid, butyl- p-hydroxy benzoic acid, benzyl alcohol, chlorhexidine or benzalkonium chloride.

86. (New) The haemostatic composition according to claim 1, wherein said composition is in the form of a sponge.

87. (New) The haemostatic composition according to claim 1, wherein said composition is in the form of a powder.

88. (New) The haemostatic composition according to claim 1, wherein said composition is in the form of flakes.

89. (New) The haemostatic composition according to claim 40, wherein said composition is in the form of a sponge.

90. (New) The haemostatic composition according to claim 40, wherein said composition is in the form of a powder.

91. (New) The haemostatic composition according to claim 40, wherein said composition is in the form of flakes.

92. (New) The haemostatic composition according to claim 42, wherein said composition is in the form of a sponge.

93. (New) The haemostatic composition according to claim 42, wherein said composition is in the form of a powder.

94. (New) The haemostatic composition according to claim 42, wherein said composition is in the form of flakes.

95. (New) The haemostatic composition according to claim 44, wherein said composition is in the form of a sponge.

96. (New) The haemostatic composition according to claim 44, wherein said composition is in the form of a powder.

97. (New) The haemostatic composition according to claim 44, wherein said composition is in the form of flakes.

98. (New) The haemostatic composition according to claim 45, wherein said composition is in the form of a sponge.

99. (New) The haemostatic composition according to claim 45, wherein said composition is in the form of a powder.

100. (New) The haemostatic composition according to claim 45, wherein said composition is in the form of flakes.